PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference ...	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/IN 03/00302	International filing date *(day/month/year)* 09.09.2003	Priority date *(day/month/year)* 18.12.2002
International Patent Classification (IPC) or both national classification and IPC C12Q1/68		
Applicant DEPARTMENT OF BIOTECHNOLOGY et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 10 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
12.07.2004	22.02.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Schmitt, C Telephone No. +49 89 2399-7351

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IN 03/00302

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1, 2, 4-10, 12-16, 19-24, 26-32	as published
3, 11, 17, 18, 25, 25a	received on 22.12.2004 with letter of 17.12.2004

Claims, Numbers

1-21	received on 22.12.2004 with letter of 17.12.2004

Drawings, Sheets

1/6-6/6	as published

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☒ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

   see separate sheet

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 21

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 21

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-20
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-20
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-20
	No:	Claims	

2. Citations and explanations

see separate sheet

Amendments

Two amended pages of sequences listing were filed with the letter dated 17.12.2004.
A first page, denoted page 25, is listing 3 different sequences which correspond to a protein sequence of 16 amino-acids and two nucleic acid sequences of 645 and 618 nucleotides, respectively.
An second page, without page number, is listing two oligonucleotides identified by SEQ ID NO: 9 and SEQ ID NO:10. This page is denoted page 25a by the International Examination Authority.

Page 25 is considered by this Authority as not fulfilling the requirements of Rule 70.2(c) PCT.
Due to the use of the expressions "Seq id no. 6 (change to 8)", "Seq id no. 7 (change to 6)" and "Seq id no. 8 (change to 7)", the sequences listed on page 25 are not clearly and unambiguously identified by a sequence name (i.e. SEQ ID NO). Therefore, in the absence of a clear and unambiguous SEQ ID NO. for each of the three sequences listed on page 25, said page is considered as introducing subject-matter which goes beyond the application as originally filed.
The present report has been established as if the amendments on page 25 had not been made.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 21 was not searched (see PCT/ISA/210). Said claim is therefore not further examined (Article 34(4)(I)(ii), Article 17(2)(a) and Rule 66.1(e) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The present application relates to the hupB gene encoding a mycobacterial histone like protein, oligonucleotide primers to amplify the hupB gene and to a method for differentiating *Mycobacterium tuberculosis* from *Mycobacterium bovis*.

Reference is made to the following documents:

D1: Prabhakar et al., "Identification of an immunogenic histone-like protein (HLPMt) of *Mycobacterium tuberculosis*.",
Tubercle and lung disease, 1998, 79, pages 43-53.
An abstract of said document has been cited in the International Search Report.
A copy of the original document is annexed to the present communication.

D2: Cohavy et al., "Identification of a novel mycobacterial histone H1 homolog (HupB) as n antigenic target of pANXA monoclonal antibody and serum immunoglobulin A from patients with Crohn's disease.",
Infection and immunity, 1999, 67, pages 6510-6517.

D3: WO99/45955, published 16 September 1999.

V.1. Novelty and inventive step of product claim 1.

Document D1 discloses (the reference in parentheses applying to this document) the identification and cloning of the hupB gene of *M. tuberculosis* (abstract and Fig. 4B). Said document also discloses two oligonucleotide primers to amplify said hupB gene which are different from the primers of Seq ID Nos 1-5 of the present application (page 45, col.2; section "PCR analysis and sequencing).

Claim 1 is therefore new in the sense of Article 33(2) PCT.

The applicant has shown that a pair of primers selected from the group consisting of Seq ID No. 1-5 has a surprising effect over primers HLPMNdeI and HLPMSalI disclosed in document D1. A pair of primers selected from the group consisting of Seq ID No. 1-5 enables the differentiation between *M. tuberculosis* and *M. bovis*. Since, this effect is not suggested by document D1, it is considered surprising over the prior art.

Claim 1 appears, therefore, to involve an inventive step in the sense of Article 33(3) PCT.

V.2. Novelty and inventive step of method claims 2-20.

None of the prior art document at hand discloses nor suggests that *M. tuberculosis* and *M. bovis* can be differentiated based on the hupB gene.
Therefore, a method for differentiating *M. tuberculosis* and *M.bovis* by amplifying a part of the hupB gene with a pair of primers selected from the group consisting of Seq ID No. 1, Seq ID No. 2, Seq ID No.3, Seq ID No. 4 and Seq ID No. 5, detecting the amplified fragment and differentiating *M. tuberculosis* from *M. bovis* based on the size of the amplified fragment appear to be new and inventive.

Thus, claims 2-20 appear to be new in the sense of Article 33(2) PCT and to involve an inventive step in the sense of Article 33(3) PCT.

Further remarks.

1. Independent claim 2 is considered to lack clarity in the sense of Article 6 PCT due its wording.
Claim 2 relates to a method for differentiating *Mycobacterium* species. From the steps defining the method of claim 2, claim 2 is defining a method for differentiating *M. tuberculosis* and *M. bovis* rather than a method for differentiating *Mycobacterium* species.

2. The expression "method according to claim 2, said *Mycobacterium* species" used in claim 3 is unclear thereby rendering the scope of said claims unclear in the sense of Article 6 PCT. Said expression appears unclear as it seems that a word (i.e. wherein) is missing.